Synthesis of Functionalized Azomethine Ylides *via* the Rh(II)-Catalyzed Cyclization of α-Diazo Carbonyls onto Imino π-Bonds

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α-Diazo carbonyl compounds containing an imino group in the γ-position have been found to undergo a rhodium(II) acetate induced cyclization reaction to generate cyclic azomethine ylides. The reactive dipole undergoes a subsequent 1,3-dipolar cycloaddition with added dipolarophiles. The imino/oxime nitrogen lone pair of electrons must be properly oriented so as to interact with the rhodium carbenoid. Thus, acyclic oxime ethers which exist in the proper *E*-configuration readily undergo the tandem cyclization–cycloaddition reaction. In sharp contrast, the isomeric *Z*-oximino diazo carbonyl system does not cyclize to an azomethine ylide but rather intramolecularly inserts into the oximino C–H bond. Addition of a catalytic amount of rhodium(II) acetate to (*E*)-2-(diazoacetyl)-benzaldehyde *O*-methyloxime in the presence of DMAD or *N*-phenylmaleimide affords a dipolar cycloadduct in high yield. When *p*-quinone was used as the dipolarophile, the initially formed cycloadduct was treated with acetic anhydride to give a compound containing the basic core dibenzo-[*a*,*d*]cyclohepten-5,10-imine skeleton found in MK-801. Cyclic imines such as isoxazolines were particularly effective substrates for azomethine ylide formation. The rhodium(II) catalyzed reaction of 3-(4-diazo-3-oxobutyl)-5-phenyl-Δ^2-isoxazoline with DMAD produced a 4:1 mixture of diastereomeric cycloadducts in good yield. Cyclization of the rhodium carbenoid did not occur with the aromatic isoxazole system and this is presumably due to the low basicity of the nitrogen lone pair of electrons.

Development of methodology for the stereocontrolled synthesis of pyrrolidine-containing natural products continues to receive significant attention.[1] Of the numerous strategies for pyrrolidine construction, 1,3-dipolar cycloaddition of an azomethine ylide across a C–C π-bond represents a particularly attractive approach.[2–6] Azomethine ylides have been extensively studied since the discovery that they can be generated by pyrolysis or photolysis of aziridines.[7–11] Other routes to azomethine ylides include the thermolysis of benzaldimines,[12] condensation of α-amino esters with carbonyl compounds,[13] reductive-ring opening of 4-oxazolines,[14] conjugate addition of *N*-alkyl imines to vinyl sulfones,[15] and the thermal 1,2-prototropy of various imines, oximes, and hydrazones.[16,17] Among the more recent methods developed for nonstabilized azomethine ylide generation, the dehydration of *N*-oxides with strong base[18] and the desilylation of α-trimethylsilyl iminium salts have drawn considerable attention.[19–25]

The addition of dihalocarbenes to C–N π-bonds to produce dihaloaziridines, presumably *via* an azomethine ylide, was uncovered by Fields and Sandri in 1959.[26]

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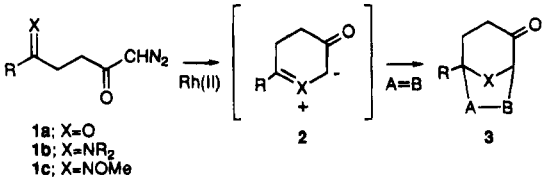
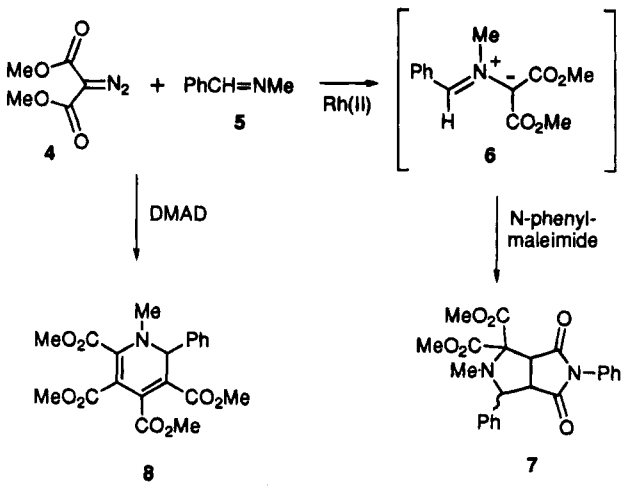
Since then a number of reports involving the insertion of carbenes into imines and the subsequent cycloaddition or rearrangement of the resulting ylide have been published.[27-29] The reaction of a metal carbenoid with a simple imine to form an azomethine ylide which then undergoes 1,3-dipolar cycloaddition with various dipolarophiles was described by Baret in 1972.[30] In that instance, ethyl diazoacetate was treated with copper bronze in the presence of excess *N*-benzylidenemethylamine, resulting in the isolation of 1,3-dimethyl-2,5-diphenylimidazoline. Bartnik and Mloston subsequently extended this observation by using other dipolarophiles.[31] For example, catalytic decomposition of phenyldiazomethane and *N*-benzylidenemethylamine in the presence of dimethyl maleate or benzaldehyde gave rise to pyrrolidine and oxazolidine cycloadducts, respectively. However, further examples using other metal carbenoids to generate azomethine ylides have been scarce.[32]

The reaction of keto carbenoids with heteroatoms which possess a lone pair of electrons is rapidly gaining prominence as an efficient method for heterocyclic synthesis.[33-41] Previous papers from these laboratories have described a route to oxapolycyclic ring systems which involves the tandem cyclization–cycloaddition reaction of a rhodium carbenoid intermediate.[42] In an effort to increase the versatility of the method, we were led to examine hetero π-systems other than carbonyl groups.[43] Of most immediate concern was the feasibility of employing α-imino diazo ketones to access cyclic azomethine ylides.[44] Cycloaddition reactions of these 1,3-dipoles should provide the 8-azabicyclo[3.2.1]octane framework found in a number of potent CNS-active agents such as cocaine and anatoxin-a.[45] In this paper we report the successful implementation of this approach as a method for generating a variety of cyclic azomethine ylides.



Results and Discussion

Bimolecular Formation of Azomethine Ylides. We initiated our investigations in this area by studying the Rh(II)-catalyzed reaction of dimethyl 2-diazomalonate (**4**) with *N*-benzylidenemethylamine (**5**) in the presence of various trapping agents. The purity of the imine was found to be extremely important since the Rh(II) catalyst is easily poisoned by free amines.[46] The reaction of dimethyl 2-diazomalonate (**4**) with imine **5** in refluxing toluene using $Rh_2(OAc)_4$ in the presence of *N*-phenylmaleimide afforded cycloadduct **7** as a 1.5:1 mixture of diastereomers. The formation of **7** involves the initial generation of azomethine ylide **6** followed by 1,3-dipolar cycloaddition across the activated π-bond present in *N*-phenylmaleimide. We also examined the reaction using dimethyl acetylenedicarboxylate (DMAD) as the trapping agent. In this case, the only compound that was isolated corresponded to dihydropyridine **8**. Apparently the reaction of imine **5** with the activated triple bond present in DMAD is faster than reaction with the small



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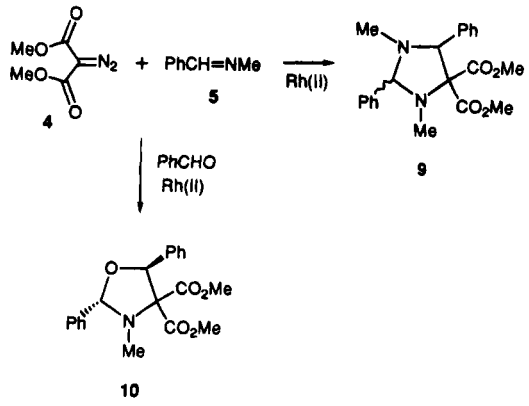
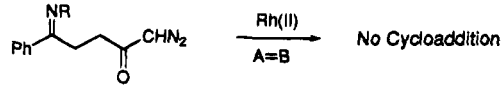
amount of the rhodium carbenoid derived from diazomalonate **4**. In the absence of an external trapping agent, the initially formed azomethine ylide **6** underwent a 1,3-dipolar cycloaddition with another molecule of imine **5** to produce the observed 1,3-imidazolidine **9** (72%, 3:1 mixture). When an equivalent amount of benzaldehyde was present, *trans*-oxazolidine **10** was obtained in 68% yield as a single diastereomer. The isolation of the above products in good yield clearly indicates that *N*-alkyl imines are capable of undergoing a rhodium(II)-induced cyclization with diazo carbonyl compounds to generate azomethine ylides.



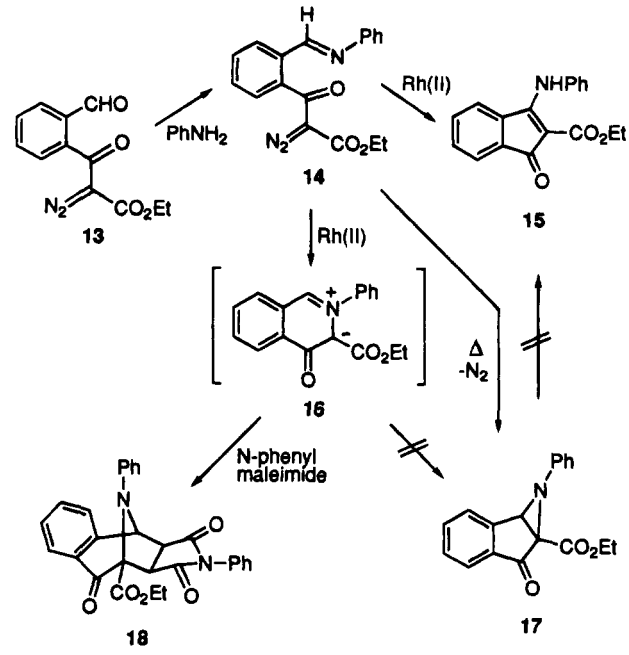
Intramolecular Formation of Azomethine Ylides. Intramolecular cyclizations have been of considerable synthetic and mechanistic interest,[47] and our long-standing involvement with the tandem intramolecular cyclization–cycloaddition reaction of α-diazo carbonyl compounds[42] prompted us to examine the analogous reaction using imino diazo ketone **11**. Unfortunately, all attempts to convert the requisite iminobutyric acid precursor to **11** failed to give product of acceptable purity. A less problematic alternative was found in the use of the methyloxime derivative **12**. In this case, conversion



11; R=CH_2Ph
12; R=OMe

of the acid to the desired diazo ketone **12** was accomplished in 65% yield using the standard diazomethane acylation protocol. Treatment of this compound with various dipolarophiles in the presence of a rhodium(II) catalyst, however, failed to give any sign of the desired cycloadduct. A possible explanation for the apparent lack of cyclization to the azomethine ylide is that the oxime ether exists in the *anti* configuration. In the absence of any *in situ* isomerization to the *syn* isomer, the nitrogen lone pair of electrons would be incapable of interacting with the rhodium carbenoid.

In order to avoid this geometric complication, we prepared the ortho-substituted *N*-phenyl imine **14** from the corresponding aldehyde **13** (see Experimental Section). The imine was obtained as a single diastereomer and was judged to exist exclusively in the proper *E*-configuration necessary for cyclization on the basis of its characteristic NMR spectral data. Treatment of **14** with $Rh_2(OAc)_4$ in benzene (80 °C) resulted in the isolation of 1-oxo-3-(phenylamino)-1*H*-indene **15** in 90% yield. The structure of compound **15** was unequivocally established by an X-ray crystal analysis.[48]



The mechanism by which **14** is converted into **15** is not so clear. One possibility involves direct insertion of the carbenoid into the imino C–H bond followed by a 1,3-hydrogen shift. An alternate route would involve formation of the expected azomethine ylide **16** followed by collapse to aziridine **17**[49] which could subsequently rearrange to **15** by an alternate path involving C–N bond cleavage.[50] In order to probe this possibility, we independently synthesized aziridine **17** by simply heating **14** in $CHCl_3$ and subjecting the resulting triazole[51] to further thermolysis which resulted in the loss of nitrogen and formation of the bicyclic aziridine **17** in 87% overall yield. When **17** was subjected to the same conditions used in the reaction of **14** [$Rh_2(OAc)_4$, 80 °C], no detectable quantities of **15** were present in the crude reaction mixture. This result strongly suggests that the formation of **15** from **14** proceeds by a CH insertion of the rhodium carbenoid directly into the imine CH bond. The cyclization of electrophilic rhodium–carbene complexes is well known to result in the preferential formation of five-membered rings in acyclic, conformationally mobile systems,[52] thereby providing excellent analogy for the direct conversion of **14** → **15**.

The Rh(II)-catalyzed reaction of **14** ($CHCl_3$) was also carried out in the presence of *N*-phenylmaleimide. Most interestingly, this reaction afforded the bimolecular cycloadduct **18** in 65% yield as well as 25% of enamide **15**. Clearly azomethine ylide formation is occurring in

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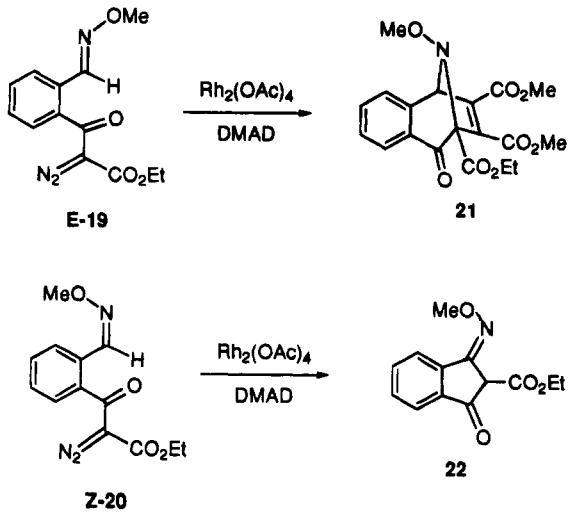
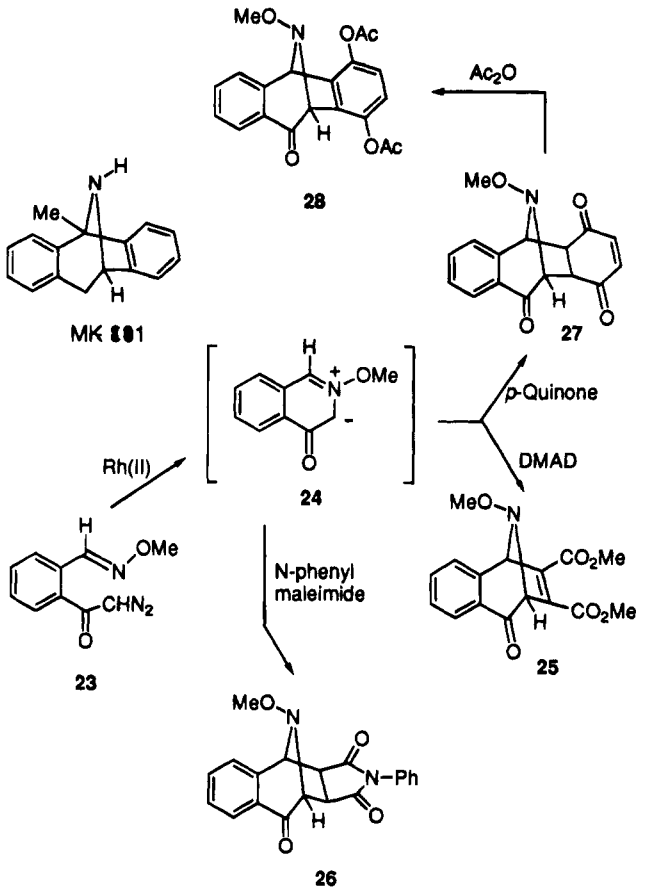
competition with CH insertion. The fact that enamide **15** is the major product in the absence of a trapping agent suggests that azomethine ylide **16** reverts back to the rhodium carbenoid which then undergoes CH insertion to produce **15**. Similar observations were made using DMAD and methyl propiolate as the added dipolarophiles.

Diazo Oxime Cyclization–Cycloaddition Reactions. The success encountered with the ortho imino system **14**, which incorporates the correct nitrogen lone pair orientation for cyclization, suggested to us that acyclic oxime ethers which exist in the proper configuration would also function as suitable azomethine ylide precursors. In contrast to *N*-alkyl imines, *O*-alkyl-substituted oximes offer the advantage of being geometrically stable at room temperature so that the *E*- and *Z*-isomers can be separated.[53] Construction of the requisite oximes was accomplished in 85% yield by treating the corresponding aldehyde **13** with *O*-methylhydroxylamine hydrochloride and separating the 5:1 mixture of *E*- and *Z*-oximino diazo ketones **19** and **20**. The geometrical assignment was made on the basis of the chemical shift of the aldoxime proton.[54] Subjection of the *E*-oximino isomer **19** to a catalytic quantity of $Rh_2(OAc)_4$ in CH_2Cl_2 (40 °C) with a slight excess of DMAD present afforded the bimolecular cycloadduct **21** in 93% yield. In sharp contrast, when the isomeric *Z*-oximino diazo derivative **20** was exposed to the same reaction conditions, only indanone oxime **22** (80%) was obtained. The formation of this product is most likely derived by an intramolecular CH insertion reaction.



The success achieved with the Rh(II)-catalyzed cycloaddition of the *E*-oximino diazo diactivated ester **19** prompted us to examine the reaction of the less activated 2-(diazoacetyl)benzaldehyde *O*-methyloxime (**23**). This diazo ketone was prepared as a single stereoisomer and is assumed to exist in the more stable *anti* configuration. Addition of a catalytic amount of $Rh_2(OAc)_4$ in the presence of a slight excess of either DMAD or *N*-phenylmaleimide provided cycloadducts **25**[55] and **26** in 80 and 64% yields, respectively. In the case of cycloadduct **26**, a 1:1 mixture of *exo*:*endo* diastereomers was obtained and easily separated by flash chromatography.[58] The cycloaddition was also performed using *p*-quinone as the dipolarophile to give cycloadduct **27** in high yield. Treatment of this material with excess acetic anhydride in pyridine afforded diacetate **28** in 67% overall yield from **23**. This latter cycloadduct incorporates the basic dibenzo[*a*,*d*]cyclohepten-5,10-imine skeleton found in MK-801,[59] which is a selective ligand for brain cyclidine (PCP) receptors that has attracted considerable recent attention as a potent anticonvulsive and neuroprotective agent.[60,61]



The oximino systems studied so far had the α-diazo carbonyl functionality attached directly to the benzene backbone. This arrangement results in a cyclic azomethine ylide, the π-system of which contributes to an aromatic ring.[62] Since we were interested in learning

(53) Curtin, D. Y.; Grubbs, E. J.; McCarty, C. G. *J. Am. Chem. Soc.* **1966**, *88*, 2775.

(54) Silverstein, R. M.; Bassler, G. C.; Morrill, T. C. In *Spectrometric Identification of Organic Compounds*, 4th ed.; Wiley: New York, 1981.

(55) The 8-azabicyclo[3.2.1]octadiene ring system **25** has a sufficiently high nitrogen barrier so that both invertomers are seen at 25 °C. The NMR spectrum of **25** contains two distinct sets of chemical shifts for the bridgehead protons and methoxylamine hydrogens. The effects of ring strain, heteroatom substitution, and restriction of the CNC angle by the cyclic ring in raising the barrier to inversion are well known.[56,57]

(56) Lehn, J. M. *Fortschr. Chem. Forsch.* **1970**, *15*, 311.

(57) Nelson, S. F.; Ippoliti, J. T.; Frigo, T. B.; Petillo, P. A. *J. Am. Chem. Soc.* **1989**, *111*, 1776.

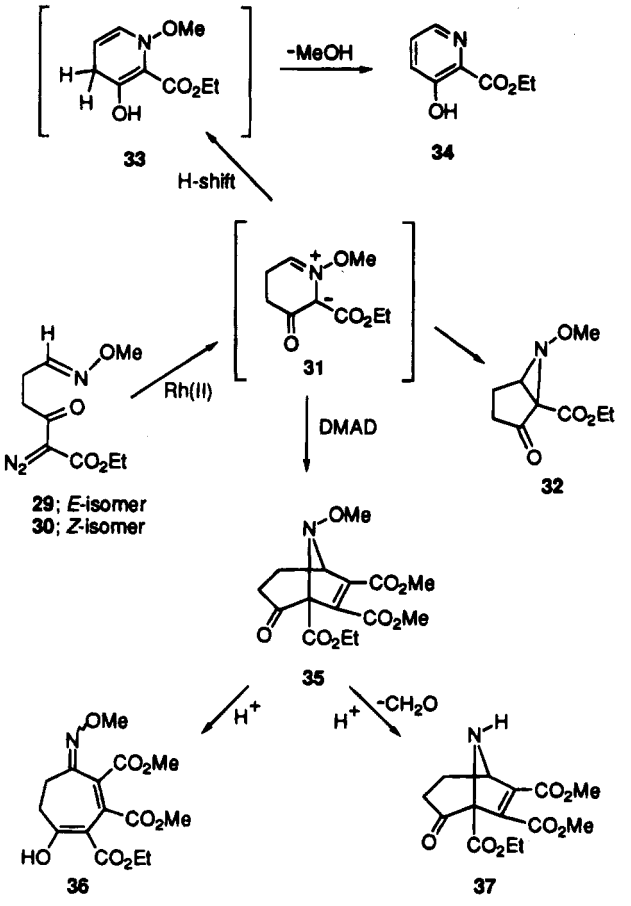
(58) The stereochemical assignment was facilitated by the appearance of the bridgehead protons of the *exo* isomer of **26** as a set of singlets in accord with a predicted dihedral angle of 90° for this diastereomer.

(59) Clineschmidt, B. V.; Martin, G. E.; Bunting, P. R. *Drug. Dev. Res.* **1982**, *2*, 123.

(60) Loo, P. A.; Braunwalder, A. F.; Williams, M.; Sills, M. A. *Eur. J. Pharmacol.* **1987**, *135*, 261.

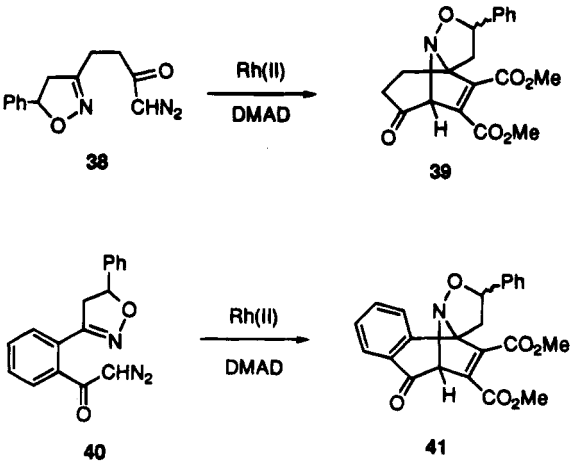
(61) McDonald, J. W.; Silverstein, F. S.; Johnston, M. V. *Eur. J. Pharmacol.* **1987**, *140*, 359.

what role this factor plays in the overall reaction pathway, we chose to study the stripped down, bare methylene system. Toward that end, the *E*- (**29**) and *Z*-oximino (**30**) diazo ketones were prepared from the known ethyl 2-diazo-6-hydroxy-3-oxohexanoate.[63] Treatment of the *E*-oximino isomer **29** with DMAD in the presence of a catalytic quantity of $Rh_2(OAc)_4$ at 25 °C produced a relatively complex reaction mixture which could be separated into three major components. The two minor products were identified as aziridine **32** (9%) and the known 2-carbethoxy-3-hydroxypyridine (**34**) (10%).[64] The formation of these compounds is readily rationalized in terms of an initially formed azomethine ylide (*i.e.*, **31**)

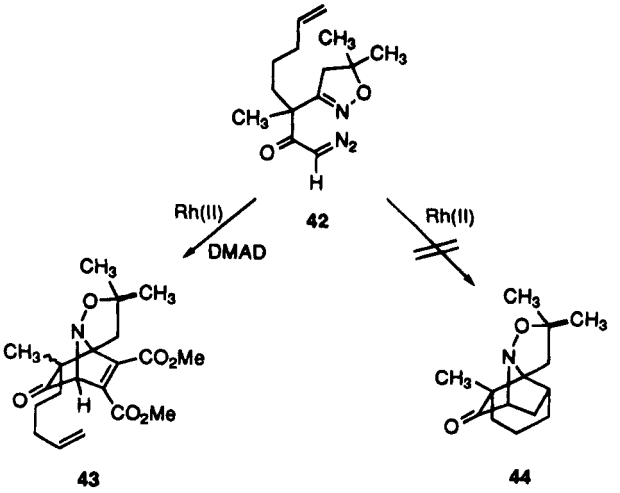


which collapses to produce aziridine **32** or undergoes a competitive proton shift followed by elimination of methanol from a transient intermediate (**33**), giving pyridine **34**. The major product isolated (55%) corresponded to cycloadduct **35**, which was not stable to silica gel chromatography. Attempts to obtain a pure sample of **35** resulted, instead, in the isolation of the ring-opened oxime **36** as well as the deformylated azabicyclo[3.2.1]-octene **37**. Treatment of the isomeric *Z*-oxime **30** under related experimental conditions did not give any detectable quantities of cycloadduct **35** or the acid-induced products (*i.e.*, **36** and **37**) derived from it. The only compounds that could be found in the crude reaction mixture corresponded to very small quantities of aziridine **32** and pyridine **34**. In contrast to the results obtained with the related *Z*-oximino benzo system **20**, we could detect no product arising from a CH insertion reaction.

Isoxazolines and Isoxazoles. The success achieved with the Rh(II)-catalyzed transformations of *E*-oximino diazo carbonyl compounds prompted us to study some additional systems where the C–N π-bond was configurationally locked so that azomethine ylide formation would readily occur. Toward this end, we elected to investigate the Rh(II)-catalyzed behavior of isoxazoline **38**. This compound was readily prepared from methyl 4-nitrobutyrate in three steps.[65] The $Rh_2(OAc)_4$-catalyzed reaction of **38** in the presence of DMAD afforded the azomethine-derived cycloadduct **39** as a 4:1 mixture of diastereomers in 65% yield. A similar transformation occurred using the α-diazoacetophenone derivative **40**[66] which produced isoxazolo[3,2-*a*]isoquinoline **41** as a 2:1 mixture of diastereomers in 82% yield.

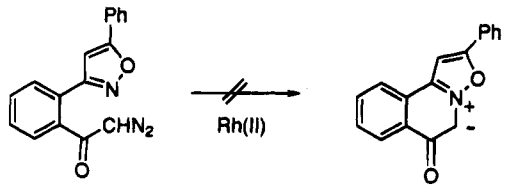


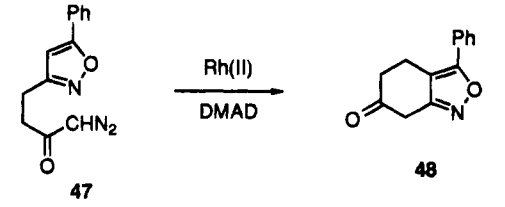
Until now, the tether length (n = 2 atoms) between the imino and diazo groups has led to cyclic six-membered azomethine ylides. Although five-ring carbonyl ylides are easily formed from the Rh(II)-catalyzed reaction of 1-diazobutanediones, the resulting dipole generally undergoes a rapid proton transfer, producing the furanone ring system.[67] In order to avoid this problem, it is necessary to block this pathway by incorporating two substituent groups into the α-position. Hence, we decided to examine the Rh(II)-catalyzed reaction of isoxazoline **42**. We were particularly interested in determining whether a tandem intramolecular cyclization–cycloaddition reaction would occur, as this would represent an extremely powerful method for synthesizing complex azatricyclic ring systems. Treatment of **42** with a catalytic amount of $Rh_2(OAc)_4$ in CH_2Cl_2 in the presence of a slight excess of DMAD afforded cycloadduct **43** as a 1:1 mixture of diastereomers in 83% isolated yield. In the absence of



DMAD, none of the anticipated intramolecular cycloadduct **44** was formed. Instead, a complex mixture of products was obtained. It is evident from the isolation of **43** that generation of five-membered-ring azomethine ylides occurs as efficiently as does their six-membered-ring counterparts. We assume that the inability of the tethered alkene to add across the azomethine ylide is due to steric constraints and/or the HOMO–LUMO gap between the unactivated alkene and azomethine ylide is too large for 1,3-dipolar cycloaddition to occur.

As part of our continuing involvement with the chemistry of azomethine ylides, we became interested in examining the cyclization of α-diazo substituted N-containing heteroaromatic systems as a method for ylide generation. Aside from some examples using pyridines,[68] isoquinolines,[29] and isoxazolidines,[69] little is known about the diazo cyclization process with N-heteroaromatic systems. This led us to explore the potential of α-diazo isoxazoles as a method for producing novel and synthetically useful dipoles. Treatment of isoxazole **45** under the standard Rh(II) cyclization conditions gave no dipolar cycloadduct. When isoxazole **47** was subjected to similar conditions, the resulting rhodium carbenoid preferred to insert into the available CH bond producing **48** in modest yield. These observations suggest that the low basicity of the isoxazole nitrogen lone pair precludes cyclization to the azomethine ylide dipole.





In conclusion, diazo-substituted imino-containing carbonyl compounds have been observed to undergo cyclization to produce azomethine ylides when treated with Rh(II) carboxylates. Cycloaddition of these dipoles with different dipolarophiles affords dipolar cycloadducts in good yield. The cyclization reaction is markedly dependent on the geometry about the imino π-bond as well as the basicity of the electron pair on nitrogen. We are continuing to explore the scope of the imino cyclization reaction and will report additional findings at a later date.

Experimental Section

Melting points are uncorrected. Mass spectra were determined at an ionizing voltage of 70 eV. Unless otherwise noted, all reactions were performed in oven-dried glassware under an atmosphere of extra dry nitrogen. Solutions were evaporated under reduced pressure with a rotary evaporator and the residue was chromatographed on a silica gel column using an ethyl acetate–hexane mixture as the eluent unless specified otherwise.

Rhodium(II)-Catalyzed Reaction of Dimethyl 2-Diazomalonate with *N*-Benzylidenemethylamine and *N*-Phenylmaleimide. The rhodium(II) acetate catalyzed reaction of 115 mg (0.66 mmol) of *N*-phenylmaleimide, 80 μL (0.66 mmol) of *N*-benzylidenemethylamine (**5**), and 89 mg (0.55 mmol) of dimethyl 2-diazomalonate (**4**) in 2 mL of toluene at 110 °C for 3 h gave a 4:3 mixture of *exo* (**7a**, 50%) and *endo* (**7b**, 34%) dimethyl 2-methyl-4,6-dioxo-3,5-diphenylhexahydropyrrolo[3,4-*c*]pyrrole-1,1-dicarboxylate. The stereochemistry was assigned by analogy with related pyrrolo[3,4-*c*]-pyrrole systems.[70] Silica gel chromatography afforded the *exo* cycloadduct **7a** as a white fluffy solid: mp 187–188 °C; IR (KBr) 1736, 1717, 1390, and 1195 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.33 (s, 3H), 3.39 (dd, 1H, J = 10.3 and 7.4 Hz), 3.80 (s, 3H), 3.93 (s, 3H), 4.11 (d, 1H, J = 10.3 Hz), 4.25 (d, 1H, J = 7.4 Hz), 7.30–7.42 (m, 6H), and 7.49–7.45 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 35.0, 50.7, 51.7, 52.6, 53.1, 70.7, 77.2, 126.5, 127.5, 128.3, 128.6, 128.9, 129.0, 131.9, 139.6, 168.1, 169.1, 173.7, and 174.9. Anal. Calcd for $C_{23}H_{22}N_2O_6$: C, 65.40; H, 5.25; N, 6.63. Found: C, 65.23; H, 5.24; N, 6.60.

The *endo* cycloadduct **7b** was obtained as small white crystals: mp 114–115 °C; IR (KBr) 1765, 1721, 1499, 1382, and 1230 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.33 (s, 3H), 3.82 (dd, 1H, J = 9.9 and 8.0 Hz), 3.86 (s, 3H), 3.89 (s, 3H), 3.95 (d, 1H, J = 8.0 Hz), 4.04 (d, 1H, J = 9.9 Hz), 7.05 (dd, 1H, J = 7.2 and 1.2 Hz), and 7.28–7.37 (m, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 35.5, 48.7, 51.2, 52.3, 52.7, 69.7, 76.4, 126.0, 128.4, 128.72, 128.74, 129.0, 131.5, 136.2, 167.09, 167.13, 173.6, and 173.8; HRMS calcd for $C_{23}H_{23}N_2O_6$ $[M]^+$ 422.1556, found 422.1556.

Rhodium(II)-Catalyzed Reaction of Dimethyl 2-Diazomalonate with *N*-Benzylidenemethylamine and Dimethyl Acetylenedicarboxylate. The rhodium(II) acetate catalyzed reaction of 160 μL (1.3 mmol) of DMAD, 160 μL (1.3 mmol) of *N*-benzylidenemethylamine (**5**), and 160 mg (1.0 mmol) of dimethyl 2-diazomalonate (**4**) in 3 mL of toluene at 110 °C for 12 h gave tetramethyl 1-methyl-6-phenyl-1,6-dihydropyridine-2,3,4,5-tetracarboxylate (**8**, 72%). Silica gel chromatography afforded **8** as bright yellow crystals: mp 160–161 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 3.00 (s, 3H), 3.61 (s, 3H), 3.63 (s, 3H), 3.80 (s, 3H), 3.85 (s, 3H), 5.45 (s, 1H), 7.26–7.38 (m, 3H), and 7.34–7.36 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 39.7, 51.7, 52.1, 52.3, 53.1, 62.8, 95.8, 108.5, 126.4, 126.7, 128.7, 128.9, 138.5, 152.6, 163.8, 164.0, 164.2, and 167.8; MS (EI) m/e 403 (M^+, 7), 372 (6), 326 (100). Anal. Calcd for $C_{20}H_{21}NO_8$: C, 59.56; H, 5.25; N, 3.47. Found: C, 59.37; H, 5.37; N, 3.44.

Rhodium(II)-Catalyzed Reaction of Dimethyl 2-Diazomalonate with *N*-Benzylidenemethylamine. The rhodium(II) acetate catalyzed reaction of 0.27 mL (2.2 mmol) of *N*-benzylidenemethylamine (**5**) and 160 mg (1.0 mmol) of dimethyl 2-diazomalonate (**4**) in 2 mL of toluene at 110 °C for 1 h gave a 3:2 mixture of *trans* (**9a**, 62%) and *cis* (**9b**, 20%) dimethyl 1,3-dimethyl-2,5-diphenylimidazolidine-4,4-dicarboxylate. The stereochemistry was assigned by analogy with related 1,3-imidazolidine systems.[31] Silica gel chromatography afforded the *trans* cycloadduct **9a** as a clear oil: IR (neat) 1734,

(62) For some related isoquinolinium imine cycloadditions, see: Padwa, A.; Vega, E. *J. Org. Chem.* **1975**, *40*, 175.
(63) Moody, C. J.; Taylor, R. J. *J. Chem. Soc., Perkin Trans. I* **1989**, 721.
(64) Shiotani, S.; Morita, H. *J. Heterocycl. Chem.* **1986**, *23*, 665.
(65) A synthetic sequence similar to that used by Pollini and coworkers was employed to prepare **38**; see: Pollini, G. P.; Barco, A.; Benetti, S.; Veronesi, B. *Synth. Commun.* **1978**, *8*, 219.
(66) Howe, R. L.; Scheppnik, F. M. *J. Heterocycl. Chem.* **1982**, *19*, 721.
(67) Padwa, A.; Chinn, R. L.; Hornbuckle, S. F.; Zhang, Z. J. *J. Org. Chem.* **1991**, *56*, 3271.
(68) Platz, M. S.; Maloney, V. M. *Kinetics and Spectroscopy of Carbenes and Biradicals;* Platz, M. S., Ed.; Plenum: New York, 1990; pp 239–252. Chen, N.; Jones, M.; White, W. R.; Platz, M. S. *J. Am. Chem. Soc.* **1991**, *113*, 4981 and references cited therein.
(69) Padwa, A.; Austin, D. J.; Precedo, L.; Zhi, L. *J. Org. Chem.* **1993**, *58*, 1144.
(70) Tsuge, O.; Kanemasa, S.; Ohe, M.; Yorozu, K.; Takenaka, S.; Ueno, K. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 4067.

1455, 1279, 1232, and 1021 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.76 (s, 3H), 2.52 (s, 3H), 3.26 (s, 3H), 3.81 (s, 3H), 4.96 (s, 1H), 5.15 (s, 1H), 7.26–7.46 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 33.5, 34.9, 51.1, 52.0, 72.1, 78.7, 86.5, 127.7, 127.8, 128.1, 128.7, 136.8, 140.3, 168.0, and 168.6; HRMS calcd for $C_{21}H_{23}N_2O_4$ [M + H]$^+$ 367.1658, found 367.1647.

The second fraction isolated from the column contained the *cis* cycloadduct **9b** as a white solid: mp 94–95 °C; IR (KBr) 1730, 1452, 1220, and 1015 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.16 (s, 6H), 3.09 (s, 3H), 3.81 (s, 3H), 3.94 (s, 1H), 4.48 (s, 1H), 7.23–7.40 (m, 2H), 7.49 (d, 1H, J = 7.2 Hz), and 7.62 (d, 1H, J = 7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 33.3, 36.5, 51.1, 51.6, 73.1, 79.3, 88.1, 127.5, 128.1, 128.4, 128.7, 129.0, 139.2, 140.2, 168.1, and 168.5; HRMS calcd for $C_{21}H_{23}N_2O_4$ [M + H]$^+$ 367.1658, found 367.1664.

Rhodium(II)-Catalyzed Reaction of Dimethyl 2-Diazomalonate with *N*-Benzylidenemethylamine and Benzaldehyde. The rhodium(II) acetate catalyzed reaction of 0.15 mL (1.52 mmol) of benzaldehyde, 0.19 mL (1.52 mmol) of *N*-benzylidenemethylamine (**5**), and 200 mg (1.27 mmol) of dimethyl 2-diazomalonate (**4**) in 3 mL of toluene at 110 °C for 3 h gave *trans*-dimethyl 3-methyl-2,5-diphenyloxazolidine-4,4-dicarboxylate (**10**, 68%) as the only diastereomer. The stereochemistry was assigned by analogy with related 1,3-oxazolidine systems.[31] Recrystallization from ether afforded white crystals of **10**: mp 102–103 °C; IR (neat) 1762, 1740, 1457, 1273, and 1222 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.04 (s, 3H), 3.20 (s, 3H), 3.80 (s, 3H), 4.56 (s, 1H), 4.90 (s, 1H), 7.28–7.43 (m, 6H), 7.54 (dd, 2H, J = 7.3 and 1.0 Hz), and 7.79 (dd, 2H, J = 7.3 and 2.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 34.6, 51.9, 52.8, 73.3, 87.6, 99.1, 128.1, 128.2, 128.8, 129.5, 135.2, 136.8, 167.3, and 168.4. Anal. Calcd for $C_{20}H_{21}NO_5$: C, 67.60; H, 5.96; N, 3.94. Found: C, 67.50; H, 5.97; N, 3.88.

Preparation and Rhodium(II)-Catalyzed Reaction of Ethyl 2-Diazo-3-oxo-3-[2-((phenylimino)methyl)phenyl]-propionate (14). Following the general procedure of Moody and Taylor,[71] a solution of 6.68 mmol of LDA in 10 mL of THF (prepared by the addition of 4.03 mL (6.68 mmol) of a 1.6 M solution of *n*-BuLi in hexane to 0.94 mL (6.68 mmol) of diisopropylamine in 10 mL of THF at 0 °C) was added dropwise to a solution of 0.87 g (7.59 mmol) of ethyl diazoacetate and 1.09 g (6.07 mmol) of 2-(dimethoxymethyl)benzaldehyde[72] in 30 mL of THF at −78 °C over 15 min. After being stirred for 2 h at −78 °C, the solution was transferred to an ice bath and the reaction was quenched with 5 mL of a pH 7 phosphate buffer solution. The reaction mixture was further diluted with phosphate buffer and extracted with CH_2Cl_2. The aqueous layer was acidified to pH 6 with 5% aqueous HCl and extracted with CH_2Cl_2. The combined CH_2Cl_2 layer was washed with water and brine, dried over Na_2SO_4, and concentrated under reduced pressure to give ethyl 2-diazo-3-(2-(dimethoxymethyl)-phenyl)-3-hydroxypropionate as a yellow oil: IR (neat) 3440, 2097, 1685, 1371, 1291, and 1107 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.29 (t, 3H, J = 7.1 Hz), 3.33 (s, 6H), 4.27 (q, 2H, J = 7.1 Hz), 5.44 (s, 1H), 6.23 (s, 1H), 7.34 (dt, 1H, J = 7.5 and 1.2 Hz), 7.41 (dt, 1H, J = 7.5 and 1.2 Hz), 7.56 (d, 1H, J = 7.5 Hz), and 7.65 (d, 1H, J = 7.5 Hz). This material was used directly in the next step without purification.

A 3.10 g (12.1 mmol) sample of $BaMnO_4$ was added to a solution of the above material in 60 mL of CH_2Cl_2, and the mixture was heated at reflux for 44 h. After being cooled to rt, the mixture was filtered through a plug of Celite and was concentrated under reduced pressure to give ethyl 2-diazo-3-(2-(dimethoxymethyl)phenyl)-3-oxopropionate as a yellow oil: IR (neat) 2143, 1726, 1693, 1308, 1269, and 1108 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.15 (t, 3H, J = 7.2Hz), 3.27 (s, 6H), 4.15 (q, 2H, J = 7.2 Hz), 5.64 (s, 1H), 7.24 (d, 1H, J = 7.7 Hz), 7.37 (t, 1H, J = 7.7 Hz), 7.44 (dt, 1H, J = 7.7 and 0.9 Hz), and 7.61 (d, 1H, J = 7.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9, 52.5, 61.2, 100.2, 126.4, 126.8, 127.7, 129.5, 135.5, 137.3, 160.5, and 188.4. The crude diazo acetal was used directly in the next step without purification.

Using a procedure similar to that used by Conia and coworkers,[73] an aqueous solution of 2.8 mL of 10% HCl was added with vigorous stirring to a suspension of 14 g of silica gel in 80 mL of CH_2Cl_2. After several minutes of stirring, a solution of the above diazo acetal in 20 mL of CH_2Cl_2 was added dropwise. The reaction mixture was stirred at rt for 3 h and then 0.8 g of solid $NaHCO_3$ was added to neutralize the mixture. After an additional 5 min of stirring, the solid phase was separated and the solvent was removed under reduced pressure. The resulting residue was subjected to flash silica gel chromatography to give 0.94 g (53% yield) of ethyl 2-diazo-3-(2-formylphenyl)-3-oxopropionate (**13**) as a yellow solid: mp 58–59 °C; IR (neat) 2147, 1717, 1698, 1636, 1320, 1258, and 1126 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.13 (t, 3H, J = 7.1 Hz), 4.09 (q, 2H, J = 7.1 Hz), 7.34 (dd, 1H, J = 7.0 and 1.8 Hz), 7.63 (m, 2H), 7.87 (dd, 1H, J = 7.0 and 1.8 Hz), and 9.99 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.0, 61.4, 127.1, 130.2, 131.4, 133.6, 133.7, 139.6, 160.5, 190.8, and 190.9. Anal. Calcd for $C_{12}H_{10}N_2O_4$: C, 58.54; H, 4.09; N, 11.38. Found: C, 58.36; H, 4.15; N, 11.33.

To a solution containing 126 mg (0.51 mmol) of **13** and excess $MgSO_4$ in 5 mL of ether was added 55 mg (0.59 mmol) of aniline. The reaction mixture was stirred at rt for 20 h, filtered, and concentrated under reduced pressure to give 161 mg of crude **14** as a yellow-orange oil: IR (neat) 2142, 1722, 1697, 1632, and 1312 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.13 (t, 3H, J = 7.0 Hz), 4.12 (q, 2H, J = 7.0 Hz), 7.13 (d, 2H, J = 7.5 Hz), 7.23 (t, 1H, J = 7.5 Hz), 7.38 (m, 3H), 7.54 (dt, 2H, J = 7.5 Hz), 7.95 (d, 1H, J = 7.5 Hz), and 8.50 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 61.4, 120.8, 126.2, 127.2, 129.1, 129.4, 130.2, 130.4, 133.6, 139.0, 151.3, 157.6, 160.7, and 188.3. Attempts to purify diazo *N*-phenyl imine **14** by a variety of chromatographic methods (silica, basic alumina) led to its partial hydrolysis, producing diazo aldehyde **13**. The crude diazo *N*-phenyl imine **14** was therefore used directly in the next step.

The rhodium(II) acetate catalyzed reaction of 100 mg (0.31 mmol) of **14** in 10 mL of hexane at 70 °C for 3 h gave ethyl 1-oxo-3-(phenylamino)-1*H*-indene-2-carboxylate (**15**, 90%): mp 159–160 °C; IR (KBr) 1683, 1642, 1609, and 1158 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.43 (t, 3H, J = 7.2 Hz), 4.39 (q, 2H, J = 7.2 Hz), 6.41 (d, 1H, J = 7.5 Hz), 7.11 (t, 1H, J = 7.5 Hz), 7.39–7.45 (m, 3H), 7.48–7.51 (m, 3H), 7.63 (d, 1H, J = 7.5 Hz), and 11.28 (brs, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.6, 60.0, 96.6, 122.1, 123.8, 126.8, 128.8, 129.7, 131.2, 132.7, 134.0, 136.8, 137.2, 167.6, 170.4, and 186.7. Anal. Calcd for $C_{18}H_{15}NO_3$: C, 73.71; H, 5.15; N, 4.78. Found: C, 73.62; H, 5.19; N, 4.77.

The rhodium(II) acetate catalyzed reaction of 134 mg (0.78 mmol) of *N*-phenylmaleimide and 200 mg (0.62 mmol) of **14** in 5 mL of $CHCl_3$ at 61 °C for 2 h gave 8-carbethoxy-*N*,10-diphenyl-5,6,7,8-tetrahydro-9*H*-benzocyclohepten-5,8-imine-6,7-*endo*-dicarboximide (**18**, 65%) as well as **15** (25%). The *endo* cycloadduct **18** was obtained as a white solid: mp 245 °C; IR (KBr) 1743, 1714, 1600, and 1187 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.14 (t, 3H, J = 6.9 Hz), 4.21 (dd, 1H, J = 9.3 and 6.9 Hz), 4.30 (q, 2H, J = 6.9 Hz), 4.68 (d, 1H, J = 9.3 Hz), 5.31 (d, 1H, J = 6.9 Hz), 6.38–6.40 (m, 2H), 6.96–7.30 (m, 9H), 7.45 (dt, 1H, J = 7.5 and 1.2 Hz), 7.56 (dt, 1H, J = 7.5 and 1.2 Hz), and 8.08 (d, 1H, J = 7.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$ + CF_3CO_2D) δ 13.3, 49.0, 51.5, 64.2, 69.1, 78.8, 121.5, 125.3, 126.1, 127.9, 128.6, 129.5, 129.6, 130.0, 130.2, 136.2, 139.3, 144.4, 167.9, 174.4, 175.4, and 189.1. Anal. Calcd for $C_{28}H_{22}N_2O_5$: C, 72.09; H, 4.75; N, 6.01. Found: C, 72.10; H, 4.63; N, 5.85.

The rhodium(II) acetate catalyzed reaction of 38 μL (0.31 mmol) of DMAD and 100 mg (0.31 mmol) of **14** in 3 mL of CH_2Cl_2 at 40 °C for 40 min gave 8-oxo-12-phenyl-12-azatricyclo-[7.2.1.0^{2,7}]dodeca-2,4,6,10-tetraene-9,10,11-tricarboxylic acid 9-ethyl ester 10,11-dimethyl ester (80%) and **15** (16%). Recrystallization from ether–hexane afforded yellow crystals of the DMAD cycloadduct: mp 105–106 °C; IR (KBr) 1755, 1734, 1721, 1694, and 1601 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.05

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(t, 3H, J = 7.2 Hz), 3.72 (s, 3H), 3.90 (s, 3H), 4.21 (m, 2H), 5.39 (s, 1H), 7.07 (m, 3H), 7.24 (m, 3H), 7.42 (m, 2H), and 8.01 (d, 1H, J = 7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.6, 52.6, 52.8, 62.3, 73.4, 87.2, 122.2, 124.6, 124.7, 127.1, 129.1, 129.4, 133.6, 141.6, 142.2, 143.0, 146.5, 161.1, 164.0, 164.3, and 183.7. Anal. Calcd for $C_{24}H_{21}NO_7$: C, 66.21; H, 4.86; N, 3.22. Found: C, 65.86; H, 4.82; N, 3.19.

The rhodium(II) acetate catalyzed reaction of 56 μL (0.78 mmol) of methyl propiolate and 200 mg (0.62 mmol) of **14** in 5 mL of $CHCl_3$ at 61 °C for 3 h gave 8-oxo-12-phenyl-12-azatricyclo[7.2.1.0^{2,7}]dodeca-2,4,6,10-tetraene-9,11-dicarboxylic acid 9-ethyl ester 11-methyl ester (73%) and **15** (11%). Silica gel chromatography afforded a pure sample of the 1:1 cycloadduct as a bright yellow oil: IR (neat) 1747, 1722, 1700, 1598, and 1277 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.28, (t, 3H, J = 7.4 Hz), 3.81 (s, 3H), 4.25–4.36 (m, 2H), 5.63 (s, 1H), 6.95–6.98 (m, 3H), 7.11–7.16 (m, 3H), 7.21 (s, 1H), 7.32–7.39 (m, 2H), and 7.88 (d, 1H, J = 7.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.0, 52.3, 62.3, 71.4, 84.0, 115.0, 120.5, 122.8, 125.0, 128.0, 128.8, 129.3, 133.7, 139.7, 142.3, 145.6, 146.5, 162.5, 164.9, and 186.1; MS (EI) m/e 377 (M$^+$, 37), 349 (24), 318 (16), and 104 (100); HRMS calcd for $C_{22}H_{19}NO_5$ 377.1263, found 377.1265.

Preparation of Ethyl 6-Oxo-1-phenyl-1a,6-dihydro-1*H*-1-azacycloprop[*a*]indene-6a-carboxylate (17). Heating a 150 mg (0.47 mmol) sample of **14** in 15 mL of $CHCl_3$ at 45 °C for 24 h gave ethyl 8-oxo-3-phenyl-3a,8-dihydro-3*H*-indeno[1,2-*d*][1,2,3]triazole-8a-carboxylate (92%): IR (neat) 1751, 1725, 1596, 1497, 1278, and 1126 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.38 (t, 1H, J = 6.9 Hz), 4.38 (q, 2H, J = 6.9 Hz), 6.00 (s, 1H), 7.17 (t, 1H, J = 7.5 Hz), 7.41–7.61 (m, 7H), and 7.87 (d, 1H, J = 7.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.0, 59.4, 63.0, 97.2, 116.5, 124.4, 124.5, 125.8, 126.4, 129.6, 130.4, 136.5, 138.5, 148.8, 165.5, and 190.8. The crude triazole was further heated in 15 mL of benzene at 80 °C for 40 h to give ethyl 6-oxo-1-phenyl-1a,6-dihydro-1*H*-1-azacycloprop[*a*]indene-6a-carboxylate (**17**, 95%): mp 113–114 °C; IR (KBr) 1745, 1729, 1595, 1489, 1277, and 1238 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.37 (t, 3H, J = 7.2 Hz), 4.40 (q, 2H, J = 7.2 Hz), 4.56 (s, 1H), 6.69 (d, 2H, J = 7.8 Hz), 6.80 (t, 1H, J = 7.5 Hz), 7.00 (t, 2H, J = 7.8 Hz), 7.24 (t, 1H, J = 7.2 Hz), 7.44 (d, 1H, J = 7.2 Hz), 7.52 (t, 1H, J = 7.2 Hz), and 7.63 (d, 1H, J = 7.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 50.0, 53.2, 62.2, 120.5, 123.1, 124.8, 127.1, 128.6, 129.3, 134.6, 134.9, 143.3, 143.9, 165.9, and 191.9. Anal. Calcd for $C_{18}H_{15}NO_3$: C, 73.71; H, 5.15; N, 4.78. Found: C, 73.66; H, 5.13; N, 4.70.

Preparation of and Rhodium(II)-Catalyzed Reaction of (*E*)- and (*Z*)-Ethyl 2-Diazo-3-oxo-3-[2-((methoxyimino)-methyl)phenyl]propionate (19 and 20). To a solution containing 200 mg (0.81 mmol) of ethyl 2-diazo-3-(2-formylphenyl)-3-oxopropionate (**13**), 100 mg of $MgSO_4$, and 100 mg of K_2CO_3 in 10 mL of ether was added 80 mg (0.93 mmol) of methoxylamine hydrochloride. The reaction mixture was stirred at 25 °C for 40 h, filtered, and concentrated under reduced pressure to give a 5:1 mixture of *E* and *Z* diazo *O*-methyloximes **19** and **20**. The residue was subjected to silica gel chromatography and the major fraction contained 162 mg (72%) of diazo *E* *O*-methyloxime **19** as a pale yellow oil: IR (neat) 2143, 1724, 1697, 1633, and 1314 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.12 (t, 3H, J = 7.1 Hz), 3.93 (s, 3H), 4.14 (q, 2H), 7.30 (dd, 1H, J = 7.5 and 1.2 Hz), 7.40 (dt, 1H, J = 7.5 and 1.2 Hz), 7.46 (dt, 1H, J = 7.5 and 1.2 Hz), 7.71 (dd, 1H, J = 7.5 and 1.2 Hz), and 8.13 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.0, 61.5, 62.2, 127.3, 129.0, 129.5, 130.3, 137.5, 146.1, 157.5, 160.5, and 187.8.

The minor fraction contained 35 mg (16% yield) of the *Z* diazo *O*-methyloxime **20** as a pale yellow oil: IR (neat) 2145, 1724, 1697, 1633, and 1305 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.19 (t, 3H, J = 7.1 Hz), 3.89 (s, 3H), 4.18 (q, 2H, J = 7.1 Hz), 7.41 (m, 2H), 7.48 (s, 1H), 7.50 (m, 1H), and 7.77 (d, 1H, J = 7.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 61.6, 62.0, 127.2, 128.3, 128.9, 129.5, 130.4, 137.8, 143.9, 160.5, and 187.1.

The rhodium(II) acetate catalyzed reaction of 43 μL (0.35 mmol) of DMAD and 88 mg (0.13 mmol) of *E*-oximino diazo ketone **19** in 8 mL of CH_2Cl_2 at 40 °C for 2.5 h gave 12-methoxy-8-oxo-12-azatricyclo[7.2.1.0^{2,7}]dodeca-2,4,6,10-tetraene-9,10,11-tricarboxylic acid 9-ethyl ester 10,11-dimethyl ester (**21**) in 93% yield: mp 138–139 °C; IR (KBr) 1739, 1726, 1706, 1644, 1598, and 1280 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.35 (t, 3H, J = 7.2 Hz), 3.69 (s, 3H), 3.75 (s, 3H), 3.87 (s, 3H), 4.40 (m, 2H), 5.37 (s, 1H), 7.40 (d, 1H, J = 7.5 Hz), 7.45 (t, 1H, J = 7.5 Hz), 7.53 (dt, 1H, J = 7.5 and 0.9 Hz), and 7.99 (d, 1H, J = 7.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.0, 52.6, 52.6, 61.4, 62.3, 74.5, 94.7, 125.6, 127.0, 129.1, 129.5, 134.5, 138.7, 140.7, 142.2, 161.8, 163.8, 164.2, and 183.0. Anal. Calcd for $C_{19}H_{19}NO_8$: C, 58.62; H, 4.92; N, 3.60. Found: C, 58.66; H, 4.97; N, 3.62.

The rhodium(II) acetate reaction of 30 mg (0.24 mmol) of DMAD and 60 mg (0.21 mmol) of *Z*-oximino diazo ketone **20** in 3 mL of CH_2Cl_2 at 40 °C for 12 h gave ethyl 3(*Z*)-(methoxyimino)-1-oxoindan-2-carboxylate (**22**) in 84% yield: mp 121–122 °C; IR (KBr) 1734, 1719, 1606, 1465, and 1028 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.33 (t, 3H, J = 7.2 Hz), 3.45 (s, 3H), 4.32 (q, 2H), 4.33 (s, 1H), 7.46 (m, 1H), 7.60 (m, 2H), and 7.69 (d, 1H, J = 7.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 55.1, 60.2, 62.2, 123.4, 126.6, 129.6, 134.7, 137.1, 140.6, 165.2, and 190.3; MS (EI) m/e 247 (M$^+$, 3), 202 (18), 157 (46), 143 (100), and 115 (93). Anal. Calcd for $C_{13}H_{13}NO_4$: C, 63.16; H, 5.30; N, 5.66. Found: C, 62.91; H, 5.37; N, 5.60.

Preparation and Rhodium(II)-Catalyzed Reaction of 2-(2-Diazoacetyl)benzaldehyde *O*-Methyloxime (23). To a solution containing 10 g (67 mmol) of 2-formylbenzoic acid in 200 mL of pyridine was added 6.4 g (77 mmol) of methoxylamine hydrochloride. The reaction mixture was stirred at 25 °C for 4 h and then the solvent was removed under reduced pressure. The residue was taken up in 1 M phosphoric acid and the aqueous solution was extracted with ether. The combined organic extracts were washed with brine and dried over $MgSO_4$ to give 10.8 g (90%) of 2-carboxybenzaldehyde *O*-methyloxime as a white solid: mp 119–120 °C; IR (KBr) 1745, 1320, and 1280 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.01 (s, 3H), 7.45 (t, 1H, J = 7.4 Hz), 7.58 (t, 1H, J = 7.4 Hz), 7.92 (d, 1H, J = 7.4 Hz), 8.11 (d, 1H, J = 7.4 Hz), 8.98 (s, 1H), and 9.25 (brs, 1H).

The above acid was treated with methyl chloroformate–triethylamine and diazomethane in the normal manner. The crude residue was subjected to silica gel chromatography to give 1.1 g (48%) of diazo *O*-methyloxime **23** as a yellow solid: mp 47–48 °C; IR (KBr) 2990, 2110, 1810, 1760, 1620, 1370, and 1180 cm^{-1}; ^{1}H NMR (90 MHz, $CDCl_3$) δ 4.01 (s, 3H), 5.65 (s, 1H), 7.45 (m, 3H), 7.95 (m, 1H), and 8.65 (s, 1H).

The rhodium(II) acetate catalyzed reaction of 0.14 mL (1.1 mmol) of DMAD and 150 mg (0.7 mmol) of **23** in 4 mL of chloroform at 25 °C gave 150 mg (80%) of dimethyl 12-methoxy-8-oxo-12-azatricyclo[7.2.1.0^{2,7}]dodeca-2,4,6,10-tetraene-10,11-dicarboxylate (**25**) as a light yellow oil: IR (neat) 1755, 1740, 1730, 1615, and 1460 cm^{-1}; high-field ^{1}H NMR showed that compound **25** exists as a 4.5:1 mixture of nitrogen invertomers at 25 °C; ^{1}H NMR (300 MHz, $CDCl_3$) (major) δ 3.65 (s, 3H), 3.76 (s, 3H), 3.79 (s, 3H), 4.95 (s, 1H), 5.25 (s, 1H), 7.40 (m, 3H), and 7.75 (m, 1H); (minor) δ 3.54 (s, 3H), 3.79 (s, 3H), 3.83 (s, 3H), 4.72 (s, 1H), 5.11 (s, 1H), 7.45 (m, 3H), and 7.75 (m, 1H); HRMS calcd for $C_{16}H_{15}NO_6$ 317.0899, found 317.0915.

The rhodium(II) acetate catalyzed reaction of **23** was carried out in the presence of *N*-phenylmaleimide at 25 °C for 2 h which resulted in a 1:1 mixture of the *exo* (**26a**) and *endo* (**26b**) 9-oxo-10-methoxy-*N*-phenyl-5,6,7,8-tetrahydro-9*H*-benzocycloheptene-5,8-imine-6,7-dicarboximide in 64% yield. Silica gel chromatography gave the *exo* cycloadduct **26a** as a white solid: mp 189–190 °C; IR (KBr) 1750, 1500, 1440, 1370, 1205, and 1085 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.35 (d, 1H, J = 7.9 Hz), 3.42 (d, 1H, J = 7.9 Hz), 3.56 (s, 3H), 4.88 (s, 1H), 5.29 (s, 1H), 7.20 (m, 2H), 7.48 (m, 5H), 7.63 (dt, 1H, J = 7.8 and 0.9 Hz), and 8.03 (d, 1H, J = 7.8 Hz). Anal. Calcd for $C_{20}H_{16}N_2O_4$: C, 68.96; H, 4.63; N, 8.04. Found: C, 69.02; H, 4.61; N, 8.12.

The *endo* cycloadduct **26b** was isolated as a colorless oil: IR (neat) 1745, 1720, 1590, 1505, 1390, and 1190 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.63 (s, 3H), 4.18 (dd, 1H, J = 8.8 and 8.6 Hz), 4.30 (dd, 1H, J = 8.8 and 7.1 Hz), 4.76 (d, 1H, J = 8.6 Hz), 5.18 (d, 1H, J = 7.1 Hz), 6.40 (m, 2H), 7.22 (m, 3H),

7.44 (m, 2H), 7.60 (t, 1H, J = 7.4 Hz), and 8.04 (d, 1H, J = 7.4 Hz). Anal. Calcd for $C_{20}H_{16}N_2O_4$: C, 68.96; H, 4.63; N, 8.04. Found: C, 68.92; H, 4.54; N, 8.03.

The rhodium(II) acetate catalyzed reaction of **23** was carried out in the presence of *p*-quinone at 25 °C for 2 h and the crude mixture was treated with 3 equiv of acetic anhydride followed by 5 equiv of pyridine and 0.1 equiv of DMAP. The solution was stirred at rt for 4 h and the solvent was removed under reduced pressure. The resulting residue was dissolved in CH_2Cl_2 and washed with 1 N HCl followed by brine and dried over $MgSO_4$, and the solvent was removed under reduced pressure. Flash silica gel chromatography gave 6,9-diacetyl-11-oxo-12-methoxy-5,10,11-trihydro-1*H*-dibenzo[*a*,*d*]cyclohepten-5,10-imine (**28**, 62%) as a light yellow solid: mp 179–180 °C; IR (KBr) 1770, 1710, 1600, 1490, 1380, and 1200 cm^{-1}; high-field ^{1}H NMR showed that compound **28** exists in solution as a 3:1 mixture of nitrogen invertomers at 25 °C; ^{1}H NMR (300 MHz, $CDCl_3$) (major) δ 2.34 (s, 3H), 2.36 (s, 3H), 3.64 (s, 3H), 5.16 (s, 1H), 5.49 (s, 1H), 7.00 (m, 2H), 7.24 (d, 1H, J = 6.5 Hz), 7.35 (t, 1H, J = 7.2 Hz), 7.52 (m, 1H), and 7.87 (m, 1H); (minor) δ 2.33 (s, 3H), 2.36 (s, 3H), 3.60 (s, 3H), 5.01 (s, 1H), 5.41 (s, 1H), 7.00 (m, 2H), 7.18 (d, 1H, J = 6.3 Hz), 7.35 (t, 1H, J = 7.2 Hz), 7.52 (m, 1H), and 7.87 (m, 1H). Anal. Calcd for $C_{20}H_{17}NO_6$: C, 65.38; H, 4.67; N, 3.81. Found: C, 65.17; H, 4.54; N, 3.63.

Preparation and Rhodium(II)-Catalyzed Reaction of (*E*)- and (*Z*)-Ethyl 2-Diazo-5-[(methoxyimino)methyl]-3-oxopentanoate (29 and 30). To a solution containing 100 mg (0.5 mmol) of ethyl 2-diazo-6-hydroxy-3-oxo-hexanoate[74] and 12 mg (0.15 mmol) of anhydrous NaOAc in 5 mL of CH_2Cl_2 was added 0.16 g (0.75 mmol) of pyridinium chlorochromate. The reaction mixture was stirred overnight at rt and then a slurry of silica gel in ether was added. The crude mixture was filtered through a plug of silica to give 80 mg (80%) of ethyl 2-diazo-3,6-dioxohexanoate as a pale yellow oil: IR (neat) 2137, 1717, 1654, 1373, and 1305 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.27 (t, 3H, J = 7.1 Hz), 2.75 (t, 2H, J = 6.2 Hz), 3.11 (t, 2H, J = 6.2 Hz), 4.24 (q, 2H, J = 7.1 Hz), and 9.75 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.0, 32.6, 37.1, 61.2, 75.6, 160.9, 190.3, and 200.0.

To a solution containing 50 mg (0.25 mmol) of the above compound, 100 mg of $MgSO_4$, and 100 mg of K_2CO_3 in 3 mL of ether was added 25 mg (0.29 mmol) of methoxylamine hydrochloride. The reaction mixture was stirred at 25 °C for 30 h, filtered, and concentrated under reduced pressure to give a 1.4:1 mixture of *E* (**29**, 40%) and *Z* (**30**, 28%) ethyl 2-diazo-5-((methoxyimino)methyl)-3-oxopentanoate. Silica gel chromatography afforded a pure sample of **29** as a pale yellow oil: IR (neat) 2137, 1717, 1656, and 1306 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.32 (t, 3H, J = 7.1 Hz), 2.52 (dt, 2H, J = 7.1 and 5.6 Hz), 3.07 (t, 2H, J = 7.1 Hz), 3.78 (s, 3H), 4.29 (q, 2H), and 7.41 (t, 1H, J = 5.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.3, 24.0, 36.9, 61.3, 61.5, 149.0, 161.3, and 191.1.

The minor *Z*-isomer **30** was also obtained as a pale yellow oil: IR (neat) 2135, 1717, 1650, and 1300 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.33 (t, 3H, J = 7.1 Hz), 2.62 (dt, 2H, J = 7.2 and 5.4 Hz), 3.05 (t, 2H, J = 7.2 Hz), 3.84 (s, 3H), 4.29 (q, 2H, J = 7.1 Hz), and 6.68 (t, 1H, J = 5.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.3, 20.3, 36.8, 61.5, 61.7, 150.0, 160.5, and 191.2.

The rhodium(II) acetate catalyzed reaction of 10 μL (0.08 mmol) of DMAD and 17 mg (0.07 mmol) of **29** in 1 mL of benzene at 80 °C for 1 h gave ethyl 2-oxo-6-phenyl-6-azabicyclo-[3.1.0]hexane-1-carboxylate (**32**, 9%), 2-carbethoxy-3-hydroxypyridine (**34**, 10%), and 8-methoxy-2-oxo-8-azabicyclo[3.2.1]oct-6-ene-1,6,7-tricarboxylic acid 1-ethyl ester 6,7-dimethyl ester (**35**, 55%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.35 (t, 3H, J = 7.2 Hz), 2.08–2.12 (m, 2H), 2.46–2.55 (m, 1H), 2.68–2.75 (m, 1H), 3.62 (s, 3H), 3.83 (s, 3H), 3.84 (s, 3H), 4.53 (q, 2H, J = 7.2 Hz), and 4.81 (dd, 1H, J = 9.3 and 3.3 Hz). Cycloadduct **35** was not stable to silica gel chromatography but its rearrangement products were isolated and characterized.

The first fraction isolated from the silica gel chromatography column contained the known pyridine **34** as a clear oil:[64] IR (neat) 3420, 1672, 1653, 1447, and 1197 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.49 (t, 3H, J = 7.2 Hz), 4.54 (q, 2H, J = 7.2 Hz), 7.37 (dd, 1H, J = 8.6 and 1.3 Hz), 7.42 (dd, 1H, J = 8.6 and 4.2 Hz), 8.29 (dd, 1H, J = 4.2 and 1.3 Hz), and 10.77 (s, 1H); MS (EI) *m*/*e* 167 (M$^+$, 10), 123 (35), 95 (100), 67 (26), and 39 (40). The second fraction contained aziridine **32** as a yellow oil: IR (neat) 1742, 1696, 1652, 1572, 1296, and 1198 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.29 (t, 3H, J = 6.9 Hz), 2.16–2.24 (m, 1H), 2.32–2.41 (m, 2H), 2.43–2.50 (m, 1H), 3.54–3.56 (m, 1H), 3.64 (s, 3H), and 4.24 (q, 2H, J = 6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 18.4, 38.1, 55.8, 58.1, 60.8, 61.8, 165.2, and 203.5; MS (EI) *m*/*e* 199 (M$^+$, 25), 174 (9), 168 (20), 154 (44), 112 (58), and 68 (100); HRMS calcd for $C_9H_{13}NO_4$ 199.0845, found 199.0849. The third fraction contained the silica gel induced rearrangment product assigned as 4-hydroxy-7-(methoxyimino)cyclohepta-1,3-diene-1,2,3-tricarboxylic acid 3-ester 1,2-dimethyl ester (**36**) as a yellow solid: mp 99–100 °C; IR (neat) 3280, 1738, 1716, 1576, 1437, and 1223 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.31 (t, 3H, J = 7.2 Hz), 2.68 (t, 2H, J = 6.3 Hz), 3.23 (t, 2H, J = 6.3 Hz), 3.68 (s, 3H), 3.77 (s, 3H), 3.89 (s, 3H), 4.28 (q, 2H), and 9.84 (brs, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 21.6, 32.7, 51.5, 52.1, 52.6, 61.6, 111.6, 119.0, 123.6, 140.7, 159.3, 163.5, 166.2, and 174.1; MS *m*/*e* 341 (M$^+$, 20), 309 (90), 281 (55), 250 (100), and 204 (88). Anal. Calcd for $C_{15}H_{19}NO_8$: C, 52.77; H, 5.61; N, 4.11. Found: C, 52.75; H, 5.54; N, 4.09. The fourth fraction contained 2-oxo-8-azabicyclo[3.2.1]oct-6-ene-1,6,7-tricarboxylic acid 1-ethyl ester 6,7-dimethyl ester (**37**) as a 3:2 mixture of rotamers: IR (neat) 3450, 1737, 1716, 1624, and 1248 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) (major) δ 1.35 (t, 3H, J = 7.1 Hz), 1.96-2.11 (m, 1H), 2.47–2.60 (m, 2H), 2.65–2.80 (m, 1H), 3.71 (s, 3H), 3.75 (s, 3H), 4.01 (d, 1H, J = 10.2 Hz), 4.40 (q, 2H, J = 7.1 Hz), and 4.60 (dt, 1H, J = 10.2 and 6.3 Hz); (minor) δ 1.25 (t, 3H, J = 7.2 Hz), 2.00–2.10 (m, 1H), 2.50–2.60 (m, 2H), 2.65–2.80 (m, 1H), 3.80 (s, 3H), 3.82 (s, 3H), 4.13–4.25 (m, 2H), 5.06 (dt, 1H, J = 8.0 and 4.2 Hz), and 5.51 (d, 1H, J = 4.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) (major) δ 13.9, 28.8, 34.8, 52.0, 52.7, 62.7, 65.1, 116.0, 137.2, 140.0, 160.3, 163.3, 171.4, and 196.1; (minor) δ 14.0, 27.8, 32.4, 52.5, 52.6, 62.2, 64.4, 115.1, 137.2, 139.5, 162.1, 167.3, 171.7, and 194.4; MS (EI) *m*/*e* 311 (M$^+$, 17), 280 (12), 252 (38), 206 (100), and 148 (93); HRMS calcd for $C_{14}H_{18}NO_7$ [M + H]$^+$ 312.1083, found 312.1083.

The rhodium(II) acetate catalyzed reaction of 12 μL (0.16 mmol) of DMAD and 27 mg (0.14 mmol) of the *Z*-oximino diazo ketone **30** in 1 mL of benzene at 80 °C for 1 h afforded pyridine **31** (6%) and aziridine **32** (4%). No sign of any DMAD cycloadduct was observed in the crude reaction mixture.

Preparation and Rhodium(II)-Catalyzed Reaction of 1-Diazo-4-(5-phenyl-4,5-dihydroisoxazol-3-yl)butan-2-one (38). A 1.0 g (4.3 mmol) sample of methyl 3-(5-phenyl-4,5-dihydroisoxazol-3-yl)propionate[75] was converted in the normal fashion to 150 mg (25% yield) of 1-diazo-4-(5-phenyl-4,5-dihydroisoxazol-3-yl)butan-2-one (**38**) as a bright yellow oil: UV (95% EtOH) 250, 271 nm (ϵ 370, 330); IR ($CHCl_3$) 2130, 1645, 1370, and 1330 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.68 (m, 4H), 2.90 (dd, 1H, J = 17.0 and 8.3 Hz), 3.36 (dd, 1H, J = 17.0 and 10.9 Hz), 5.31 (brs, 1H), 5.52 (dd, 1H, J = 10.9 and 8.3 Hz), and 7.25–7.35 (m, 5H); HRMS calcd for (M − N_2) $C_{13}H_{13}NO_2$ 215.0946, found 215.0944.

The rhodium(II) acetate catalyzed reaction of 23 μL (0.19 mmol) of DMAD and 43 mg (0.18 mmol) of **38** in 3 mL of chloroform at 25 °C for 4 h gave 40 mg (65%) of dimethyl 7-oxo-3-phenyl-4-oxa-5-azatricyclo[4.3.2.0^{1,5}]undec-10-ene-10,11-dicarboxylate (**39**) as an inseparable 4:1 mixture of diastereomers: IR (neat) 1740, 1655, 1445, 1340, 1275, and 1240 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) (major) δ 2.07 (m, 1H), 2.40 (m, 3H), 2.69 (m, 1H), 3.20 (dd, 1H, J = 12.9 and 7.6 Hz), 3.80 (s, 3H), 3.96 (s, 3H), 4.78 (s, 1H), 5.30 (dd, 1H, J = 8.0 and 7.6 Hz), and 7.38 (m, 5H); (minor) δ 2.10 (m, 1H), 2.40 (m, 3H), 2.70 (m, 1H), 3.00 (dd, 1H, J = 12.1 and 7.4 Hz), 3.94 (s, 3H), 3.94 (s, 3H), 4.83 (s, 1H), 5.20 (dd, 1H, J = 7.9 and 7.4 Hz), and 7.28 (m, 5H); HRMS calcd for $C_{19}H_{19}NO_6$ 357.1212, found 357.1223.

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Preparation and Rhodium(II)-Catalyzed Reaction of 2-Diazo-1-[2-(5-phenyl-4,5-dihydroisoxazol-3-yl)phenyl]-ethanone (40). A procedure similar to that used by Howe and co-workers[76] was employed to prepare methyl 2-(5-phenyl-4,5-dihydroisoxazol-3-yl)benzoate. To a stirred solution containing 4.15 g (19 mmol) of methyl 2-((chlorohydroxyimino)-methyl)benzoate[76] and 4.05 g (39 mmol) of styrene in 60 mL of ether was added dropwise 2.85 mL (20 mmol) of triethylamine in 10 mL of ether over 45 min with stirring at 0–5 °C. The mixture was stirred at 20 °C for 12 h and was then washed with three 50 mL portions of water. The ether layer was dried over $MgSO_4$, and the solvent was removed under reduced pressure. The resulting residue was subjected to flash silica gel chromatography to give 3.5 g (65%) of methyl 2-(5-phenyl-4,5-dihydroisoxazol-3-yl)benzoate as a colorless oil: IR (neat) 1735, 1435, 1305, 1275, and 1110 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.32 (dd, 1H, J = 16.6 and 8.7 Hz), 3.63 (dd, 1H, J = 16.6 and 10.8 Hz), 3.80 (s, 3H), 5.80 (dd, 1H, J = 10.8 and 8.7 Hz), 7.43 (m, 8H), and 7.95 (d, 1H, J = 7.1 Hz).

To a solution containing 1.85 g (46 mmol) of NaOH and 5.5 mL of water in 23 mL of methanol at 100 °C was added the above ester, and the mixture was stirred at 100 °C for 15 min. The solvent was removed under reduced pressure, diluted with water, and acidified to pH 3 with concentrated HCl. The acidic solution was extracted with ethyl acetate, and the organic layer was dried over $MgSO_4$ and concentrated under reduced pressure to give 1.35 g (78%) of 2-(5-phenyl-4,5-dihydroisoxazol-3-yl)benzoic acid as a pale yellow solid: mp 147–148 °C; IR (KBr) 3150, 1705, 1430, 1295, and 890 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.36 (dd, 1H, J = 16.6 and 8.7 Hz), 3.75 (dd, 1H, J = 16.6 and 10.8 Hz), 5.80 (dd, 1H, J = 10.8 and 8.7 Hz), 7.52 (m, 8H), 8.05 (d, 1H, J = 7.4 Hz), and 10.20 (brs, 1H).

The above carboxylic acid was converted in the normal fashion to 2-diazo-1-[2-(5-phenyl-4,5-dihydroisoxazol-3-yl)phenyl]ethanone (**40**, 67%), isolated as a light yellow solid: mp 46–47 °C; IR (KBr) 3040, 2120, 1630, and 1370 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.32 (dd, 1H, J = 16.7 and 8.3 Hz), 3.74 (dd, 1H, J = 16.7 and 10.8 Hz), 5.58 (s, 1H), 5.78 (dd, 1H, J = 10.8 and 8.3 Hz), and 7.50 (m, 9H).

The rhodium(II) acetate catalyzed reaction of 43 μL (0.35 mmol) of DMAD and 93 mg (0.3 mmol) of **40** in 3 mL of chloroform at 25 °C for 30 min gave 107 mg (83%) of a 3:1 mixture of the diastereomers of dimethyl 2-phenyl-8-oxo-3,-3a,8,9-tetrahydro-2*H*-3a,9-ethenoisoxazolo[2,3-*a*]isoquinoline-11,12-dicarboxylate (**41**): IR (neat) 1755, 1740, 1730, 1460, 1445, and 1275 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) (major) δ 2.80 (dd, 1H, J = 12.7 and 8.3 Hz), 3.65 (dd, 1H, J = 12.7 and 7.7 Hz), 3.79 (s, 3H), 3.81 (s, 3H), 5.21 (s, 1H), 5.38 (dd, 1H, J = 8.3 and 7.7 Hz), 7.50 (m, 8H), and 8.01 (m, 1H); (minor) δ 3.02 (dd, 1H, J = 13.0 and 6.6 Hz), 3.22 (dd, 1H, J = 13.0 and 8.9 Hz), 3.73 (s, 3H), 3.80 (s, 3H), 5.26 (s, 1H), 5.30 (dd, 1H, J = 8.9 and 6.6 Hz), 7.51 (m, 8H), and 8.02 (m, 1H); HRMS calcd for $C_{23}H_{19}NO_6$ 405.1212, found 405.1210.

Preparation and Rhodium(II)-Catalyzed Reaction of 1-Diazo-3-(5,5-dimethyl-4,5-dihydroisoxazol-3-yl)-3-methylhept-6-en-2-one (42). To 16.3 g (95.0 mmol) of formyl Meldrum's acid[77] in 200 mL of benzene was added 8.5 g (10.8 mL, 0.11 mol) of *tert*-butyl alcohol. This mixture was heated at reflux for 3 h. After being cooled to 25 °C, the mixture was concentrated under reduced pressure. To this residue was added a mixture of 7.3 g (0.10 mol) of $NaHCO_3$ in 200 mL of H_2O. The mixture was stirred at 25 °C for 12 h and then diluted with 400 mL of CH_2Cl_2. The organic layer was washed with 50 mL of an aqueous $NaHCO_3$ solution and 50 mL of brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give 14.7 g (100%) of a 1.3:1 mixture of *E*/*Z* *tert*-butyl ((hydroxyimino)methyl)acetate. The crude aldoximes were used without further purification: IR (neat) 3450, 1723, 1631, 1370, and 1161 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.51 and 7.02 (t, 1H, J = 7.5 Hz), 3.26 (d, 2H, J = 7.5 Hz), and 1.45 (s, 9H).

Following the procedure of Torssell,[78] into a threaded pressure tube at −78 °C was condensed 30 mL of 2-methylpropene and 7.0 g (49.0 mmol) of *N*-chlorosuccinimide and 0.25 mL of pyridine in 15 mL of $CHCl_3$ was added. To this mixture was added a solution of 7.0 g (49.0 mmol) of the above crude *E*/*Z* aldoximes in 15 mL of $CHCl_3$ followed by the slow addition of 6.8 mL (49.0 mmol) of triethylamine. The threaded pressure tube was sealed and warmed to 25 °C. After 6 h of stirring, the threaded pressure tube was cooled to −78 °C, opened, and allowed to slowly warm to 25 °C. The mixture was diluted with 400 mL of ether and washed with 100 mL of an aqueous NH_4Cl solution and 100 mL of brine. The organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Silica gel chromatography afforded 2.88 g (28%) of *tert*-butyl (5,5-dimethyl-4,5-dihydroisoxazol-3-yl)acetate as a clear oil: IR (neat) 1723, 1370, 1328, 1281, and 1156 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.40 (s, 6H), 1.45 (s, 9H), 2.79 (s, 2H), and 3.31 (s, 2H).

To a solution containing 0.8 mL (5.63 mmol) of *N,N*-diisopropylamine at 0 °C was added 3.2 mL of a 1.6 M solution of *n*-BuLi in hexane. The thick syrup was cooled to −78 °C and 20 mL of THF was added. To this solution was added 0.2 mL (1.17 mmol) of HMPA followed by 1.0 g (4.69 mmol) of the above ester in 5 mL of THF. This mixture was stirred at −78 °C for 0.5 h. To this solution was added 1.2 mL (9.40 mmol) of 5-bromo-1-pentene, and this mixture was slowly warmed to 25 °C. The reaction was quenched with 10 mL of saturated aqueous NH_4Cl, and the solution was diluted with 100 mL of ether. The organic phase was washed with 25 mL of an aqueous NH_4Cl solution and 25 mL of brine. The organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Silica gel chromatography afforded 0.97 g (74%) of *tert*-butyl 2-(5,5-dimethyl-4,5-dihydroisoxazol-3-yl)-hex-5-enoate as a clear oil: IR (neat) 1723, 1631, 1459, and 1254 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.39 (d, 3H, J = 4.5 Hz), 1.45 (s, 9H), 1.65 (m, 1H), 1.89 (m, 1H), 2.08 (m, 2H), 2.70 (AB, 2H, J = 16.8 Hz, $\Delta\nu$ = 28.1 Hz), 3.42 (t, 1H, J = 7.7 Hz), 5.0 (m, 2H), and 5.78 (m, 1H).

To 1.15 mL (8.23 mmol) of *N,N*-diisopropylamine at 0 °C was added 4.3 mL of a 1.6 M solution of *n*-BuLi in hexane. The thick syrup was cooled to −23 °C, and 90 mL of THF was added. To this solution was added 0.3 mL (1.72 mmol) of HMPA followed by 1.93 g (6.86 mmol) of the above ester in 10 mL of THF. The mixture was stirred at −78 °C for 45 min. To this solution was added 2.1 mL (34.3 mmol) of methyl iodide, and the mixture was stirred at −23 °C for 2 h and slowly warmed to 25 °C. This reaction was quenched by the addition of 25 mL of aqueous NH_4Cl, and the solution was diluted with 250 mL of ether. The ether layer was washed with 50 mL of aqueous NH_4Cl and 50 mL of brine. The organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Silica gel chromatography afforded 1.50 g (73%) of *tert*-butyl 2-(5,5-dimethyl-4,5-dihydroisoxazol-3-yl)-2-methylhex-5-enoate as an oil: IR (neat) 3079, 1723, 1631, 1460, 1370, and 1254 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.38 (s, 6H), 1.45 (s, 9H), 1.50–1.20 (m, 2H), 1.70 (td, 1H, J = 12.8 and 5.0 Hz), 1.90 (td, 1H, J = 13.0 and 5.1 Hz), 2.04 (q, 2H, J = 7.0 Hz), 2.66 (AB, 2H, J = 16.5 Hz, $\Delta\nu$ = 27.5 Hz), 4.95 (m, 2H), and 5.57 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.2, 23.5, 27.9, 33.8, 35.4, 47.0, 48.4, 81.3, 84.0, 114.9, 138.1, 160.2, and 172.7.

A solution containing 0.59 g (2.0 mmol) of the above ester in 10 mL of a 4:1 mixture of CH_2Cl_2/TFA was stirred at 25 °C for 2 h. This mixture was concentrated under reduced pressure, and the resulting carboxylic acid was converted in the normal fashion to 0.39 g (74%) of 1-diazo-3-(5,5-dimethyl-4,5-dihydroisoxazol-3-yl)-3-methylhept-6-en-2-one (**42**) as a yellow oil: IR (neat) 2100, 1642, 1351, and 912 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.40–1.30 (m, 9H), 1.80 (m, 4H), 2.05 (q, 2H, J = 7.0 Hz), 2.62 (AB, 2H, J = 16.8 Hz, $\Delta\nu$ = 22.3 Hz), 4.95 (m, 2H), 5.32 (s, 1H), and 5.78 (m, 1H); ^{13}C NMR (75 MHz,

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$CDCl_3$) δ 19.4, 23.3, 27.0, 27.2, 33.9, 34.9, 46.8, 51.6, 53.3, 84.5, 115.1, 138.0, 160.5, and 195.0.

The rhodium(II) acetate catalyzed reaction of 81 mg (0.57 mmol) of DMAD and 75 mg (0.29 mmol) of **42** in 5 mL of CH_2Cl_2 at 25 °C for 1.5 h gave dimethyl 9-but-3-enyl-3,3,9-trimethyl-10-oxo-4-oxa-5-azatricyclo[4.2.2.$0^{1,5}$]dec-7-ene-7,8-dicarboxylate (**43**). Silica gel chromatography afforded 89 mg (83%) of cycloadduct **43** as a 1:1 mixture of inseparable diastereoisomers: IR (neat) 1767, 1718, 1642, 1438, 1318, and 1279 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.15, 1.22, and 1.31 (s, 9H), 1.36 and 1.39 (s, 9H), 2.01–1.40 (m, 4H), 2.24 (AB, 2H, J = 12.6 Hz, $\Delta\nu$ = 77.6 Hz), 2.24 (AB, 2H, J = 12.6 Hz, $\Delta\nu$ = 118.7 Hz), 3.74 (s, 3H), 3.79 (s, 3H), 4.58 and 4.60 (s, 1H), 4.93 (m, 2H), and 5.70 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.1, 21.3, 23.6, 24.0, 26.2, 26.4, 29.5, 29.6, 33.5, 34.1, 34.6, 36.4, 40.0, 40.7, 47.0, 48.5, 52.4, 52.5, 75.7, 76.2, 85.7, 85.8, 91.3, 92.1, 114.8, 115.0, 131.1, 132.2, 137.7, 138.0, 152.2, 152.5, 162.2, 164.7, 164.8, 205.3, and 205.6. Anal. Calcd for $C_{20}H_{27}NO_6$: C, 63.63; H, 7.21; N, 3.71. Found: C, 63.56; H, 7.04; N, 3.63.

Preparation of 2-Diazo-1-[2-(5-phenylisoxazol-3-yl)-phenyl]ethanone (45). 2-(5-Phenylisoxazol-3-yl)benzoic acid[76] was treated with methyl chloroformate–triethylamine and diazomethane according to the general procedure used for the preparation of α-diazo ketones, and this resulted in a 73% yield of diazo isoxazole **45** as a yellow oil: IR (neat) 2120, 1735, 1625, 1405, and 1365 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 5.50 (s, 1H), 6.80 (s, 1H), 7.62 (m, 7H), and 7.95 (m, 2H). All attempts to obtain dipolar cycloadducts derived from an azomethine ylide failed to lead to any characterizable products.

Preparation and Rhodium(II)-Catalyzed Reaction of 1-Diazo-4-(5-phenylisoxazol-3-yl)butan-2-one (47). A solution containing 0.83 g (3.6 mmol) of methyl 3-(5-phenylisoxazol-3-yl)propionate[79] was converted in the normal fashion to 0.15 g (26% overall yield) of diazo isoxazole **47** as a light yellow powder: mp 116–117 °C; IR ($CHCl_3$) 2115, 1640, 1450, 1375, and 1220 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.79 (m, 2H), 3.05 (m, 2H), 5.32 (brs, 1H), 6.38 (s, 1H), 7.44 (m, 3H), and 7.74 (m, 2H). The rhodium(II) acetate catalyzed reaction of 26 μL (0.21 mmol) of DMAD and 45 mg (0.19 mmol) of **47** in 2 mL of benzene at 25 °C for 1 h gave 3-phenyl-5,7-dihydro-4*H*-benz[*c*]isoxazol-6-one (**48**, 60%): IR ($CHCl_3$) 1725, 1455, and 1440 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.74 (t, 2H, J = 7.1 Hz), 3.19 (t, 2H, J = 7.1 Hz), 3.66 (s, 2H), 7.42–7.51 (m, 3H), 7.68–7.70 (m, 2H). Anal. Calcd for $C_{13}H_{11}NO_2$: C, 73.21; H, 5.20; N, 6.57. Found: C, 73.16; H, 5.08; N, 6.41.

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Supplementary Material Available: Copies of ^1H and ^{13}C NMR spectra (75 MHz) of compounds lacking analyses (10 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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